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SYSTEMATIC REVIEWS AND META-ANALYSES

Laparoscopic surgery during the COVID-19 pandemic: detection of SARS-COV-2 in abdominal tissues, fluids, and surgical smoke

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Abstract

Background There are still concerns over the safety of laparoscopic surgery in coronavirus disease 2019 (COVID-19) patients due to the potential risk of viral transmission through surgical smoke/laparoscopic pneumoperitoneum.

Methods We performed a systematic review of currently available literature to determine the presence of severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) in abdominal tissues or fluids and in surgical smoke.

Results A total of 19 studies (15 case reports and 4 case series) comprising 29 COVID-19 patients were included. The viral RNA was positively identified in 11 patients (37.9%). The samples that tested positive include the peritoneal fluid, bile, ascitic fluid, peritoneal dialysate, duodenal wall, and appendix. Similar samples, together with the omentum and abdominal subcutaneous fat, tested negative in the other patients. Only one study investigated SARS-COV-2 RNA in surgical smoke generated during laparoscopy, reporting negative findings.

Conclusions There are conflicting results regarding the presence of SARS-COV-2 in abdominal tissues and fluids. No currently available evidence supports the hypothesis that SARS-COV-2 can be aerosolized and transmitted through surgical smoke. Larger studies are urgently needed to corroborate these findings.

Keywords COVID-19 · Surgery · Surgical smoke

Introduction

The safety of laparoscopic surgery (LS) in the currently ongoing coronavirus disease 2019 (COVID-19) pandemic is still unclear due to concerns of possible disease transmission via surgical smoke/laparoscopic pneumoperitoneum [1–3]. The expression of angiotensin-converting enzyme 2 (ACE2) in the gastrointestinal tract [4] and prolonged fecal shedding of severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) in COVID-19 patients [5] suggest that the gastrointestinal tract may serve as a site of viral entry and replication. Moreover, gastrointestinal symptoms are common in COVID-19, with abdominal pain and nausea/vomiting reported to be associated with increased odds of progression to severe disease [6].

It has been theorized that the use of energy devices such as monopolar and bipolar electrocautery during LS may result in the aerosolization of SARS-COV-2 [2, 7, 8]. The relatively stagnant heated volume of gas created by laparoscopic pneumoperitoneum may allow concentration of the virus [9], to which the surgeon and operating room staff may be exposed during port insertion or removal, exchange of laparoscopic instruments, specimen retrieval, or evacuation of pneumoperitoneum at the end of the procedure. This theory is supported by previous studies in which viruses such as hepatitis B virus (HBV) [10], human papillomavirus virus (HPV) [11], and human immunodeficiency virus 1 (HIV-1) [12] could be detected in vapors created by power surgical instruments.

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The aerosolization of SARS-COV-2 would require the virus to be present intraperitoneally in the first place. Therefore, we performed a systematic review of currently available literature to determine if SARS-COV-2 is present in abdominal fluids or tissues and in surgical smoke generated during abdominal surgery on COVID-19 patients.

Methods

Study protocol and registration

This systematic review was conducted in conformity with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines [13] (Supplementary material 1). The protocol for this study was registered on PROSPERO, an international prospective database for systematic reviews (Registration no. CRD42020200078).

Literature search strategy

A comprehensive and systematic search of literature from inception to 11 February 2021 was conducted on the electronic databases MEDLINE (PubMed interface), Hinari (Health InterNetwork Access to Research Initiative), and China National Knowledge Infrastructure (CNKI) to identify the studies eligible for inclusion. The electronic search was carried out using the strategy as follows: (SARS-COV-2) AND ((((abdominal tissues) OR (peritoneal fluids)) OR (bile)) OR (surgical smoke)). No language restriction was applied. When the articles were published by the same study group and there was an overlap of the search period, only the most recent article was included to avoid duplication of data. The PubMed function "related articles" was used to extend the search. We also searched major surgical and infectious disease journals reporting articles about COVID-19 infection to look for additional studies. We then performed hand-search of the bibliography of included studies, to detect other potentially eligible investigations.

Eligibility criteria

Search results were screened by title and abstract, with those of potential relevance evaluated by full text. Studies were deemed eligible for inclusion if they fulfilled the following criteria: (1) clinical studies on patients with a confirmed diagnosis of COVID-19 and (2) investigated the presence of SARS-COV-2 in patients' abdominal fluids (peritoneal fluid/bile/ascitic fluid/peritoneal dialysate) or abdominal tissue (bowel wall, adipose tissue). Exclusion criteria were the following: (1) studies with incomplete or unclear data and (2) studies reporting SARS-COV-2 tests on samples other than the ones outlined in the inclusion criteria.

Data extraction and quality assessment

Data extraction was conducted by two independent reviewers (I.C, P.S). For each study, the following information was extracted: the surname of the first author and the year of publication, the geographical region where the study was performed, the type of study, age and sex composition of the patients, type of surgical procedure, nature of the procedure (elective or emergency), types of samples tested, type of test performed, and the outcome of the test. Any variances were resolved by a consensus. Quality assessment and analysis of risk of bias of all selected full-text articles were performed using the methodological index for non-randomized studies (MINORS) tool.

Outcomes of interest

The primary outcome of interest was the presence of SARS-COV-2 RNA in abdominal fluids and tissues. The secondary outcome was the presence of SARS-COV-2 RNA in surgical smoke generated during abdominal surgery.

Results

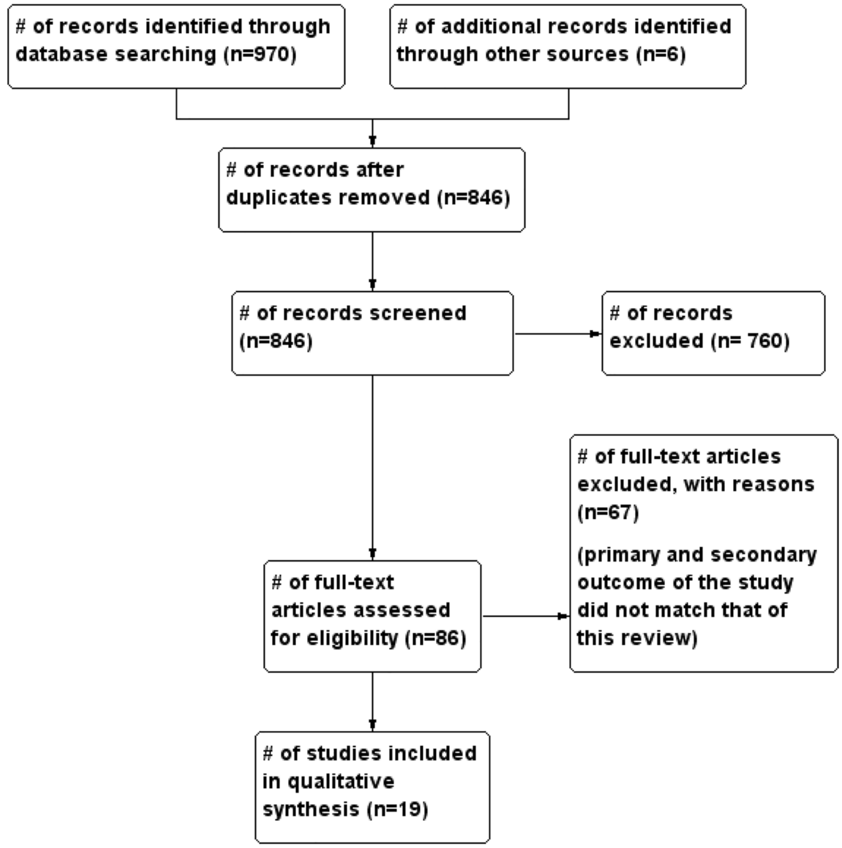
Study identification

The initial search produced 976 potentially relevant articles. Following the removal of duplicates and primary screening, 86 articles were assessed by full text for eligibility. Of these, 67 were excluded because the primary and secondary outcome of the study did not match that of this review. Thus, a total of 19 articles were included in this systematic review (Fig. 1 and Table 1).

Characteristics of the included studies and quality assessment

A total of 19 studies (n = 29 COVID-19 patients) were included [14–32]. These patients were diagnosed with COVID-19 on the basis of positive reverse transcriptase–polymerase chain reaction (RT-PCR) in oropharyngeal and/or nasopharyngeal swabs in 17 studies. The other two utilized anti-SARS-COV-2 immunoglobulin G (IgG) assay [29] and chest CT scan [30]. Fifteen were case reports, while 4 were case series. Of the included studies, 11 were from Europe, 5 from Asia, 1 from the Middle East, and 2 from the Americas. The essential characteristics of the included studies are outlined in Table 1. A summary of the MINORS assessment for the included studies is provided in Supplementary material 2.

Fig. 1 Flow of studies through the meta-analysis



Presence of SARS-COV-2 in abdominal fluids and tissues of COVID-19 patients

The abdominal fluids and tissues tested across the 19 studies included the peritoneal fluid [14, 20, 22, 24, 25, 28], peritoneal dialysate [21, 31, 32], ascitic fluid [17, 19, 26], bile [15, 17, 18, 27, 30], small bowel and appendix [16, 29], liver and gallbladder [16, 17], and visceral fat (omentum and abdominal subcutaneous tissues [16] (Table 2). All studies tested for SARS-COV-2 presence using reverse transcriptase–polymerase chain reaction (RT-PCR), but none assessed the presence of viable particle with cytopathic studies. Overall, the positive identification of SARS-COV-2 RNA was reported in 11 out of the 29 patients (37.9%) included in this review. The time from diagnosis of COVID-19 to testing of various abdominal tissues/samples was reported in 12 studies, and it ranged from 0 to 63 days (Table 1).

The largest study was a case series of 5 surgical patients (bowel resection, appendectomy, rectosigmoid resection, and drainage of hemoperitoneum) from Strasbourg, France [14]. Peritoneal fluid samples were obtained both at the beginning and at the end of the operation in three patients and only at the beginning in two patients. The fluid samples tested negative for SARS-COV-2 in all patients [14]. In another case series of 4 surgical patients from Tehran, Iran, SARS-COV-2 RNA was detected in the duodenal wall of the patient with perforated peptic ulcer. The peritoneal fluid of this patient was however negative for the virus, as were multiple samples (small bowel wall, appendix, gallbladder, bile, liver, visceral fat (omentum), abdominal subcutaneous tissue) from the other 3 patients [16]. Similarly, Scutari and colleagues [27] in their study successfully identified SARS-COV-2 in two patients with acute cholecystitis.

The rest of the studies were single-patient case reports, with 8 reporting cases of successful detection of SARS-COV-2 in abdominal samples. Han and colleagues [18] reported a case of a 59-year-old patient with severe COVID-19 requiring mechanical ventilation and a history of liver transplantation. The patient developed biliary obstruction during admission, treated with endoscopic retrograde cholangiopancreatography (ERCP) and nasobiliary drainage. Bile samples from this patient tested using real-time fluorescent RT-PCR were positive for SARS-COV-2 RNA [18]. Culver et al. [19] described the case of a 71-year-old patient admitted to the intensive care unit due to severe upper gastrointestinal bleed requiring endoscopic treatment. After an initial recovery phase, the patient subsequently developed severe respiratory distress and rapidly deteriorated. Ultrasound performed during diagnostic imaging for COVID-19 revealed large ascites, which upon drainage tested positive for SARS-COV-2 RNA [19]. The third study with positive RNA detection was published by Coccolini and colleagues [22], who detected SARS-COV-2 in peritoneal

Table 1 Characteristics of the included studies and summary of findings

Author	Setting	Study design	No. of patients	Age and sex	COVID-19 status at time of procedure	Surgical procedure	Sample collected	Time from COVID-19 diagnosis to specimen collection	Test performed	Outcome of the test	SARS-COV-2 in stool	Filtration devices used
Seeliger [14]	Strasbourg, France	Case series	5	3 M, 2 F; 44–71 yrs	NP swabs positive for 4 patients, negative for one patient	Open bowel resection, lap appendectomy, open rectosigmoid resection, open drainage of hemoperitoneum	Peritoneal fluid	9, 1, 24, 1, and 25 days respectively	RT-PCR (threshold limit of detection: 10 copies/reaction)	Negative in all cases	Not tested	Not reported
Ying [15]	Zhejiang, China	Case report	1	F, 68 yrs	Positive on NP swabs	Ultrasound-guided percutaneous transhepatic gallbladder drainage	Bile	13 days	RT-PCR	Negative	Positive	Not reported
Safari [16]	Tehran, Iran	Case series	4	3 M, 1 F; 30–75 yrs	Positive on NP swabs	Lap cholecystectomy, small bowel resection, and anastomosis, open appendectomy, stomach, and duodenal repair + gastrojejunostomy	Bowel wall, appendix, gallbladder, bile, liver, visceral fat (omentum), and abdominal subcutaneous fat	2 days and 7 days (NR in 2 patients)	RT-PCR	Positive in the duodenal wall of one patient, negative in the rest	Positive in 3 cases	Not reported
Flemming [17]	Wuerzburg, Germany	Case report	1	NR	Positive on NP swabs	Cholecystectomy	Abdominal fluid (ascites), bile, liver, and gall bladder samples	NR	RT-PCR	Negative	Negative	Not reported
Han [18]	Hangzhou, China	Case report	1	M, 59 yrs	Positive on NP swabs	Endoscopic retrograde cholangiopan-creatography	Bile	23 days	RT-PCR	Positive	Positive	Not reported
Culver [19]	Marseille, France	Case report	1	M, 71 yrs	Positive on NP swabs	Ascitic fluid drainage	Ascitic fluid	NR	RT-PCR	Positive	Not tested	N/A
Ngaserin [20]	Singapore	Case report	1	M, 21 yrs	Positive on NP swabs	Laparoscopic appendectomy	Peritoneal fluid	NR	RT-PCR	Negative	Not tested	Not reported
Vischini [21]	Rome, Italy	Case report	1	F, 53 yrs	Positive on NP swabs	Peritoneal dialysis	Peritoneal dialysate	30 days	RT-PCR	Positive	Not tested	N/A
Coccolini [22]	Pisa, Italy	Case report	1	M, 78 yrs	Positive on NP swabs	Adhesiolysis	Peritoneal fluid	1 day	RT-PCR	Positive	Not tested	Not reported
Romero-Velez [23]	New York, USA	Case report	1	NR	Positive on NP swabs	Laparoscopic appendectomy	Peritoneal fluid and surgical smoke	NR	RT-PCR	Negative	Not tested	Not reported
Kabir [24]	Sengkang, Singapore	Case report	1	NR	Positive on NP swabs	Laparoscopic subtotal cholecystectomy	Peritoneal fluid and bile	9 days	RT-PCR	Negative	Not tested	Not reported

Table 1 (continued)

Author	Setting	Study design	No. of patients	Age and sex	COVID-19 status at time of procedure	Surgical procedure	Sample collected	Time from COVID-19 diagnosis to specimen collection	Test performed	Outcome of the test	SARS-COV-2 in stool	Filtration devices used
						with open conversion						
Barberis [25]	Italy	Case report	1	F, 71 yrs	Positive on OP swabs	Subtotal colectomy with terminal ileostomy	Peritoneal fluid	NR	RT_PCR	Positive	Not tested	Not reported
Passarelli [26]	Sao Polo, Brazil	Case report	1	M, 75 yrs	Positive on NP swabs	Ascitic fluid drainage	Ascitic fluid	2 days	RT-PCR	Positive	Positive	N/A
Scutari [27]	Rome, Italy	Case series	2	M, 80 yrs; M, 74 yrs	Positive on NP swabs	Cholecystostomy	Bile	46 and 63 days, respectively	RT-PCR	Positive in both cases	Positive In both cases	N/A
Agnes [28]	Rome, Italy	Case report	1	M, 72 yrs	Positive on NP swabs	Open omentoplasty for duodenal ulcer repair	Peritoneal fluid	12 days	RT-PCR	Negative	Positive	N/A
Ahmad [29]	London, UK	Case report	1	M, 28 yrs	Positive on IgG assay	Open appendectomy	Appendix	NR	RT-PCR	Positive	Not tested	N/A
Liao [30]	Wuhan, China	Case report	1	F, age not provided	Positive on chest CT scan	ERPC, sphincterotomy, lithotripsy, and nasobiliary drainage	Bile	NR	RT-PCR	Positive	Negative	N/A
Candellier [31]	Brussels, Belgium	Case series	3	2 M, 1 F; 60, 53, and 68 yrs	Positive on NP swabs	Peritoneal dialysis	Peritoneal dialysate	0 days	RT-PCR	Negative	Not tested	N/A
Sadioglu [32]	Ankara, Turkey	Case report	1	F, 62 yrs	Positive on NP and OP swabs	Peritoneal dialysis	Peritoneal dialysate	12 h	RT-PCR	Negative	Not tested	N/A

Table 2 Results of SARS-COV-2 testing of various tissues across the included studies

Samples		Study	
		Positive	Negative
Abdominal tissues	Small bowel	(16)	N/A
	Appendix	(29)	(16)
	Gallbladder/liver	N/A	(16, 17)
	Omentum	N/A	(16)
Abdominal fluids	Bile	(18, 28, 31)	(15, 16, 17
	Peritoneal fluid	(22, 25)	(14, 17, 20, 23, 24, 30)
	Peritoneal dialysate	(21)	(26, 27)
	Ascitic fluid	(19, 32)	N/A
Surgical smoke		N/A	(23)

fluid of a 78-year-old patient undergoing adhesiolysis for small bowel obstruction. In the fourth study by Vischini et al. [21], the virus was identified in peritoneal dialysate of end-stage renal disease of a patient undergoing peritoneal dialysis. The fifth study by Barberis [25] successfully detected the viral RNA in the peritoneal fluid of a 71-year-old undergoing subtotal colectomy with terminal ileostomy. In the other 2 studies, SARS-COV-2 RNA was positively identified in the bile [30] and ascitic fluid [26] of COVID-19 patients. The remaining 9 studies did not identify SARS-COV-2 RNA in the abdominal tissues (liver and gallbladder) or fluid (bile and peritoneal fluid/dialysate/brushings) of COVID-19 patients [14, 15, 17, 20, 23, 24, 28, 31, 32].

Out of the 11 patients with positive findings of SARS-COV-2 in abdominal tissues/fluids, 9 had corresponding positive nasopharyngeal swabs, while two patients (diagnosed with COVID-19 on the basis of chest CT [30] and IgG assays [29]) had negative nasopharyngeal swabs.

Presence of SARS-COV-2 in surgical smoke generated during abdominal surgery

We identified only one study investigating the presence of SARS-COV-2 RNA in surgical smoke generated during abdominal surgical procedures [23]. Romero-Velez and colleagues [23] collected surgical smoke during laparoscopic appendectomy on a COVID-19 patient. The virus was however not identified within the smoke using real-time RT-PCR.

Discussion

The COVID-19 pandemic has had a significant impact on the delivery of surgical services to patients worldwide. Guidelines from surgical societies recommended postponement of elective surgical procedures [1, 33]. Nonetheless, the need to perform emergency and oncological surgery on both COVID-19 patients and non-COVID-19 patients still remained [17, 24]. As laparoscopic surgery is an established treatment modality in surgery [34, 35], and with the gradual resumption of elective surgeries, the risk of virus transmission through surgical smoke/laparoscopic pneumoperitoneum remains an issue of great concern.

Summary of evidence, strengths, and limitations

In this systematic review, we found that there exist conflicting results on the presence of SARS-COV-2 RNA in abdominal tissues and fluids. We identified 10 reports in which SARS-COV-2 could be successfully identified in the peritoneal fluid, peritoneal dialysate, bile, ascitic fluid, duodenal wall, and appendix of COVID-19 patients [16, 18, 19, 21, 22, 25–27, 29, 30] (Table 2). Similar samples however tested negative for the virus in another 9 studies. Only one study tested for the presence of the virus in laparoscopic surgical smoke, and it reported negative findings [23].

That being said, these findings should be interpreted with caution due to several reasons. First, all studies included in this review utilized RT-PCR to detect SARS-COV-2 RNA. This technique of testing has been shown to yield "false negative" in up to 40% of the upper respiratory tract specimens of COVID-19 cases [36]. Therefore, it cannot be ruled out that nucleic acid amplification tests (NAATs) may also miss to accurately identify the virus in some abdominal tissues and fluids due to a number of pre-analytical and analytical issues, as described in details by Lippi and colleagues [37]. Second, as the test does not usually distinguish infectious from noninfectious virus [38], the potential infectivity of the contaminated abdominal samples remains unknown. It is noteworthy that none of the studies attempted to demonstrate the presence of a live virus in the samples through techniques such as viral culture and cytopathic studies, so as to provide stronger evidence of infectivity. Third, the possibility of false-positive cases due to sample contamination was not entirely ruled out in some of the cases included in this review. Contamination of samples may occur through sub-optimal skin preparation or from fecal material, which have been shown to contain SARS-COV-2 RNA in up to 54% of COVID-19 patients, as well as from surgical blood, especially in patients with severe illness who may frequently have viremia [39]. Fourth, the studies that were included in this review were either case reports or small case series, which investigated different samples from patients with different pathologies and undergoing different procedures. As such, this introduces significant heterogeneity in results and compromises on generalization. Future studies should take into consideration the above-mentioned issues so as to provide stronger evidence of intraperitoneal viral contamination and risk of viral transmission via laparoscopic surgical smoke.

Although current evidence does not support the hypothesis that SARS-COV-2 can be aerosolized and transmitted through surgical smoke, practical measures to mitigate any theoretical risk are recommended. These include proper use of personal protective equipment within the operating room, limiting the presence of staff during intubations and induction of anesthesia, safe evacuation of all pneumoperitoneum/surgical smoke using ultrafiltration systems, as well as complete evacuation of pneumoperitoneum prior to specimen extraction or conversion to open surgery [8, 40]. This is crucial, considering the rising number of new infections in many countries, the risk of nosocomial COVID-19 infection (of up to 15%) [41], and the current widespread unavailability of COVID-19 vaccines.

This is, to the best of our knowledge, the first systematic analysis of the presence of SARS-COV-2 virus in abdominal tissues, fluids, and laparoscopic surgical smoke. We believe our findings are relevant in the formulation of future guidelines for the management of COVID-19 requiring abdominal surgical interventions, especially at a time when resumption of elective surgical procedures have already begun [42, 43].

Conclusions

There are conflicting results regarding the presence of SARS-COV-2 in abdominal tissues and fluids. No currently available evidence supports the hypothesis that SARS-COV-2 can be aerosolized and transmitted through surgical smoke. Larger studies are urgently needed to corroborate these findings.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00423-021-02142-8.

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Declarations

Conflict of interest The authors declare no competing interests.

Research involving human participants and/or animals This article does not contain any studies with human participants performed by any of the authors.

Informed consent This article does not contain any studies with human participants performed by any of the authors.

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